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Abstract

Oncologists need to recognise the need to move beyond the ECOG Performance Status score (ECOG PS). ECOG PS is a longstanding and ubiquitous feature of oncology. It was evolved 40 years ago as an adaption of the 70-year-old Karnofsky score. It is short, easily understood and part of the global language of oncology. The wide prevalence of ECOG PS attests to its proven utility and worth to help triage patient treatment.

The ECOG PS is problematic. It is a unidimensional functional score. It is mostly physician assessed, subjective and therefore open to bias. It fails to account for multimorbidity, frailty or cognition. Too often the PS is recorded only once in wilful ignorance of a patient's changing physical state.

As modern oncology offers an ever-widening array of therapies that are 'personalised' to tumour genotype modern oncologists must strive to better define patient phenotype. Using a wider range of scoring and assessment tools oncologists can identify deficits which may either be reversed or steps taken to mitigate detrimental effects of treatment. These tools can function well to identify those patients who would benefit from comprehensive assessment. This article identifies the strengths of PS but highlights the weaknesses and where these are supported by other measures. A strong recommendation is made here to move to routine use of the Clinical Frailty Score to start to triage patients and most appropriately design treatments and rehabilitation interventions.

The safe and effective practice of oncology asks of us that we classify the cancer using appropriate tools. We must then assess the treatment options in the context of the patient's ability to tolerate them. Achieving the optimum therapeutic ratio requires that our patient fitness meets a threshold. The long-established shorthand for that fitness has been the ECOG Performance Status (PS); a synthesised scale of symptoms and mobility. The ECOG has been around for a long time, its development from the 70 year-old Karnofsky score (KPS) [1] is summarised in a single paragraph of less than 50 words from a paper written 40 years ago [2] which describes how the percentage based Karnofsky was further simplified into a five point scale.

In those intervening decades the ECOG PS has become the common and international language of oncology practice allowing a swift shorthand which is shared between teams and in research communication.

There is much to recommend the ECOG PS and its' impressive longevity attests to a broad utility. The simplicity of a six-point scale has assisted its ubiquity. When compared directly with KPS (a meta-analysis of studies where HCPs completed both assessments) KPS may perform better [3] although the 5 point simplicity of the ECOG-PS may be easier for patients to understand and HCPs to remember. That same simplicity contributes to low interobserver variability [4] and agreement between members of the multidisciplinary team [5]. The scale can also be completed by patients themselves with high physician concordance in reporting their functional status [6, 7]. In the modern era ECOG PS recording can also be done effectively and accurately with wearable technologies [8].

The ECOG PS has gone on to prove both prognostic and predictive utility. The score has shown to align closely to benefit in the use of cytotoxic chemotherapy in lung cancer [9] and in that context strongly influences treatment decisions in lung cancer chemotherapy [10]. It helps prognosticate in a palliative care setting [11] and can predict for depression [12] . ECOG PS is widely used in UK oncology and in an recent survey 90% of healthcare professionals managing older patients with cancer used it as part of their assessment [13]. The primacy of ECOG PS is such that it would be rare to see peer reviewed research in print which did not report the score of treated cohorts. It is also used widely in regulatory frameworks and guidance. In the UK it used to filter funding for novel cancer therapies. As of March 2020, there are 44 unique drugs (supporting 64 indications for solid tumours) on the NHS England Cancer Drug Fund list. All but two of have strictures around ECOG PS that limit prescribing (three requiring "sufficient PS", 14 requiring a PS of at least 2 and the remainder needing the patient to demonstrate a PS of 0 or 1). There are no other indicators

of fitness required in any of the listings [14]. The Cancer Drug Fund list is dominated by drugs of eye-watering cost and in that context it may be surprising that the only functional assessment required of the patient before prescribing is a 5 point scale.

Given this prevalence of ECOG PS in cancer a curious aspect is that it has not been more widely adopted outside of oncology, apart from some very limited early uptake in renal and geriatric medicine; as an assessment of function, it has predictive mortality in older adult (non-cancer) inpatients with pneumonia [15] .

Problems with PS

Although ECOG PS use is widespread it is still far from universal. There are still a substantial number of clinicians who will make a decision to use chemotherapy despite poor PS [10]. ECOG PS often does not reach the multidisciplinary team meeting where treatment decisions are discussed; in a recent study of UK practice only 14% of such discussions included information about patient fitness [16]. This may not be a problem with the scale as much as a problem of the team not recognising the need for functional assessment.

Despite the long pedigree of PS it has significant problems. The useful simplicity of the ECOG PS also is one of its' major drawbacks. It lacks granularity, particularly around the (often crucial) decision nexus at Performance Status 2. The score contains no weighting as to whether the impairment in function is musculoskeletal or due to organ dysfunction (e.g. cardiac or respiratory). The PS lacks any dimension to assess the impact of cognition or mood and no heed of patient social status or attitudes. Consider the cases of two men with the same diagnosis and ECOG PS but with widely different physical reserve, functional capability and medical histories (See FIG 1.) It would not surprise oncology professionals if these two patients had very different experiences with cancer therapy despite having the same ECOG PS score.

Everyday usage of ECOG PS assumes that the risk-benefit ratio of a given treatment will change according to the points on the scale, with caution required with higher scores due to higher risk. There is a paucity of evidence to support differential outcomes according to ECOG PS and the exclusion of patients of poor PS means that subgroup analysis is usually not possible. When ECOG PS is reported in clinical trial work it is most often as a clinical

feature of the cohorts and occasionally as a variate in terms of benefit; it is only rarely reported as a variate with respect to toxicity. A meta-analysis of over 100 RCTs showed that whilst 60% reported PS subgroups for analysis of efficacy none did so for toxicity. This does not help us challenge long held biases, very particularly around a ECOG PS threshold of 2 [17].

Physician Bias

There are other problems too; the score is (predominantly) physician assessed and therefore subjective and prone to bias [18]. It may vary according to the quality of history taken/provided. Vignette studies have shown discrepant PS scoring between healthcare professionals was significantly influenced by the provided background social information with these differences most obvious in the decision threshold region around a PS score of 2 [19]. Overestimation of PS is not uncommon and when there is discordance between patient and physician over scoring it associated with poorer prognosis in both solid tumours [7, 20, 21] and in haematological malignancies [22] In a UK lung clinic physician assessed PS had poor predictive ability for whether or not a patient would complete planned treatment (although patient self-rated PS was more usefully predictive) [23].

Working with patients to design the best treatment course relates directly to how physicians make decisions. Decision making will be influenced by contextual factors (the environment in which the decision is made), decision-maker related characteristics (the biases and behaviours of the decision maker as a person) and decision specific elements (the nature of the decision itself) [24] . The impression of a patient's functional status may be formed differently according to context and interpreted differently according to decision

maker behaviours. How that functional status assessment is implemented may depend on decision specific elements. All of these elements are too vulnerable to biases and variation in estimate if we rely on a tool as basic and subjective as ECOG PS. As we grow our evidence base this too needs to be supported by a greater granularity in understanding treatment effects according to functional status.

There have been attempts to refine and improve the ECOG PS. The Palliative Performance Scale which includes assessments of self-care, nutritional intake and conscious level [25] shows utility in prognosticating towards end of life . The Palliative Prognostic Index (PPI) utilizes the PPS, oral intake, dyspnoea at rest, and delirium to predict 3-week and 6-week survival. The Palliative Prognostic (PaP) Score uses clinical prediction of survival, KPS, anorexia, dyspnoea and white cell metrics to predict 30-day survival in patients with advanced cancers [26]. A further adaptation accounts for delirium [27]. Here the ECOG PS score has mutated in purpose from predicting fitness for treatment to preparedness for end of life but it is recognised that PS is recorded to a lesser degree once initial treatment has been determined and even less so as a patient progresses through advanced stage of disease into palliative care [28]. In palliative radiotherapy scores have been developed that use other factors (including site of metastasis, previous radiotherapy, tumour type) added to the ECOG PS or KPS) to produce a score that may assist in identifying with those most likely to benefit from the treatment (Chow Score) [29, 30]. These scores have been adapted because of the limitations of the performance score and all have some proven utility in the specific scenarios for which they have been developed. Adapted performance scores do not help us fulfil a brief for a tool that provides valuable information across the wider spectrum of all cancer diagnoses, stages and treatments.

Changing Paradigms

When Karnofsky and Burchenal designed their original performance score in 1949 it was as part of a textbook for the nascent science of chemotherapy. Chemotherapy has changed significantly since then and is far from the only therapeutic paradigm in regular usage. Immunotherapy, radiotherapy and surgical oncology trials have all adopted ECOG PS as a routine baseline assessment. These developing modalities may demand less (or more) of patient fitness. Immunotherapy in particular is a treatment that can appear well tolerated unless toxicities develop. The evolution of toxicity appears independent of performance status. This has led to critical reviews of the ECOG PS as a triage tool for immunotherapies, particularly in lung cancer where many patients are assessed as PS 2 or lower at presentation. Meta-analyses of immunotherapy have shown similar overall survival gains regardless of PS [31, 32] although they are problematic as they take data from trials which included only small numbers of patients of poor PS [33]. Also trials of immunotherapy may show similar ORR benefits regardless of PS but this may not be enough to overcome the survival disadvantage of poor PS at the outset [34]. There are also signals that despite the overall survival gains in lung cancer immunotherapy appearing to be agnostic of patient PS this may not be true for all subgroups. This may be particularly the case in older patients where some outcomes still appear to be driven by poor PS (despite immunotherapy) [35]. These data illustrate that PS does not give us enough information on its own in our current era.

Changing populations

It is not only treatment options that are evolving; populations are shifting too.
As our populations age and our control of chronic diseases improve, we increasingly deal with the patient with multimorbidities and polypharmacy. Our current systems have evolved around single specialities which are a poor fit for the patient with multi-morbidities. The concept of multi-speciality "Cluster Medicine" [36] has been proposed but, as yet, oncology seems poorly prepared to adopt this model as training and practice and continue to enshrine specialism over generalism. It is in our current era of the older patient and the patient with multimorbidity that the ECOG PS is shown to be most deficient.
One important way to move beyond performance status is to look instead at frailty. Frailty is a multidimensional concept that will encompass many of the issues that also inform Performance Status. Frailty is variably defined but recognises that an individual may not be able to recover to their functional baseline if physically stressed and is a consequence of cumulative decline in many physiological systems [37].

It is crucial to understand that multimorbidity, age and frailty are independent; a patient may be older but not frail, have multimorbidities and not be older. Frailty and multimorbidity will overlap [38]. Clinicians will normally intuitively understand that not all older patients are unfit and that ageing and multimorbidity are not universally entwined. What matters is not the enumeration of calendar years or past diagnoses but a focused assessment of fitness. Frailty is likely to be a more helpful term for use by cancer multidisciplinary teams than age as it more specifically focuses on what a patient with cancer is likely to be able to tolerate when receiving treatment.

Beyond Performance Status

Performance status is a reductive assessment of function but there are multiple ways to enhance this to provide more granular analysis. To tailor therapy most effectively for the potentially frail patient we need to look beyond performance status and explore the domains of health characterised in Table 2. We may at the very least ask that ECOG PS be combined with some other scales of physical performance and ability that would give a less one-dimensional view of the patient's ability and function.

ECOG PS also gives a 'label' for a patient with no suggestion that there may be room for optimisation or reversibility. To work better, our scores need to identify patients who will benefit from treatment and also identify those that will not whilst predicting complications. It should be sensitive enough to be able to detect issues not found by routine history and physical examination in the initial evaluation. It should take account of geriatric syndromes and problems (delirium, falls, pressure ulcers, constipation) as well as smoking, alcohol excess, vision problems, social isolation and loneliness

Reviews that address polypharmacy with subsequent medical optimisation may well improve functional status - such as optimisation of hypothyroidism or reduction in opiates. Frailty is a dynamic state which can improve with intervention; pre frailty can respond to exercise, calorie review, protein diet and vitamin D supplementation [39]. The simple act of combining a geriatric screening tool such as the G8 will improve the utility of the PS [40]

One simple triage test would be to use an ECOG PS 2 or higher to trigger a next level of assessment –to focus on the true significance of any deficit to function (and whether there is reversibility). A list of useful tools for each of the domains under consideration is given in Table 2

A significant problem with the ECOG PS is that it does not allow well to adjust for functional difficulties that predate the cancer. A careful history of ability to complete the basic skills of self-care as activities of daily living (ADLs) should be standard. The instrumental activities of daily living (IADLs) are those which are required to maintain independence e.g. shopping, laundry, paying bills and using the telephone/internet. ADLs/ IADLs will broadly correlate with ECOG PS and share similar characteristics in being able to identify poorer prognosis [41]. Nonetheless the IADL/ADL history should be an indispensable part of placing the patient in a domestic and societal context. Other functional scores include The Barthel index (BI). The ASA used by surgical colleagues gives information which performs similarly well [42] as does the Edmonton Frail Scale which has been recommended in the elective surgical setting [43].

It is important to acknowledge that for many healthcare professionals scoring systems are not always popular. Although awareness of scoring systems was relatively high amongst UK cancer professionals there has been little enthusiasm to use them [13]. One might speculate that a score is antithetical to a clinician's belief in the 'art' of diagnostic medicine. Whatever the reason for clinician's dislike of scoring systems studies which demonstrate utility would hopefully become persuasive.

An improvement on performance status scoring would be a scale that would allow for greater granularity than ECOG PS and would account for cognitive issues.

Physical functioning may be more objectively assessed in the clinic. A comprehensive number of tests are available but the need for a shorthand in clinic has long been recognised. Assessment of function may be performed in a number of brief physical tasks;

these include measures of hand grip strength [44] or gait speed [45]. One in three patients with slow gait speed will be frail. Physical tests can be combined with a brief timed element for greater differential estimations, these include 2-Minute Step Test, 30-Second Sit to Stand, Timed Arm Curl, and the Timed Up and Go [46]. All of these tests may be conducted relatively quickly in any normal clinic scenario and (with the exception of grip strength) without specialist equipment. The names of the tests themselves indicate that they can be performed in seconds or minutes. The ability to have these tests available is not limited by equipment, space or time but by the willingness of the clinical team to accept them as useful. Tests may be combined to increase the range of function tested e.g. the Short Physical Performance Battery measures a patient's gait speed, balance and timed sit-to-stand the test has a high predictive power in identifying patients most likely to complete chemo , overall prognosis and physical decline [23, 47, 48]. Physical functioning may be combined with short functional questions; the PRISMA 7 questionnaire is a simple seven item questionnaire to identify disability, has been used in earlier frailty studies and is also suitable for postal completion. (and may be combined with TUG or gait speed for improved accuracy) [49]

A review of all the available tools to assess and quantify frailty and its' domains is beyond the scope of this article and has been comprehensively performed by other authors [50-52]. The modern oncologist needs to have insight into these tools and understand when and where they should be effectively deployed in screening their patients.

These tests do not take a long time; validation studies show that screening tests can be completed in less than half an hour with two thirds of that time spent by patient or caregiver in completing tests and 5-6 minutes required by the healthcare provider [53-55].

When we compare this with the amount of time that the patient will spend on diagnostic testing prior to treatment or the costs of that treatment itself claiming that there is "no time" to complete functional assessments begins to look indefensible [56]. Baseline echocardiography, DPD deficiency testing or renal function assessment may all be part of routine protocol in chemotherapy delivery alongside complex and expensive imaging technology in staging. Adding more detailed functional and frailty assessment should be considered similarly necessary.

For therapies that carry low burden or for patients who are fit then ECOG PS continues to be an adequate basic assessment. In many of these cases an ECOG PS will tell the treating team enough to know that it is reasonable to proceed with standard of care. Accepting that PS has a 'green light' function also commits us to accept that it may also point to amber or red and in these situations, a further detailed review is required. That review may best take the form of a comprehensive assessment – most often seen in older adults as a Comprehensive Geriatric Assessment or CGA. A CGA is not a score or a number, but a multi-disciplinary process that identifies medical, psychosocial, and functional limitations of a frail person which then leads to a coordinated plan to maximise potential for health and tackle reversible issues [57, 58]. In contrast to the scores described here a CGA is a process and intervention rather than a simple enumeration of potential issues. A fuller assessment using the domains that ae regular part of a CGA are likely to identify issues that are also routinely detected in a PS. For an assessment to have a beneficial purpose it must identify reversible elements of frailty particularly those that are likely to influence treatment decisions. A Comprehensive Geriatric Assessment therefore becomes a valid use of resources when it may meaningfully influence the oncology decision at hand.

It is not surprising that in such a detailed process an adequate PS may hide problems which can be identified by CGA [59]. These benefits of CGA would seem obvious and international guidance for management of older cancer patients recommends the process as a standard [52] [60] [61] .

In the UK however only 15% of UK oncology healthcare professionals included geriatricians in care of patients “often or always” [13] and with very significant workforce issues greater demand for CGA may quickly outstrip supply [62]. It is not likely to be possible anytime soon to offer comprehensive assessment for all. Under these circumstances it is reasonable to propose ECOG PS as permissive for fitter, younger patients and to use more instructive tools and scores to identify and triage those who may benefit from a comprehensive assessment. When CGA is not accessible, practical or possible the simple example of adding a G8 to baseline assessment still improve prognostic certainty and allow for better and safer triage of patients [63]

PS is an observed scale of function; it was not intended to reflect on patient reported outcomes. Although PS can correlate with Quality of Life [64] it was not designed to do so, quality of life measures however can, if correctly recorded, give valuable information around function and outcome. Patients reporting PROMS can outperform ECOG PS as a predictor of survival as can a formal assessment of quality of life [18, 65, 66] . In older patients incorporating a patient reported tool like the Vulnerable Elders survey as part of the early assessment would be helpful- a simple screening tool that can be administered by non-medical personnel in approximately 4 minutes in person or over the telephone [67] .

Tools and Calculators

Extra information gathered as part of a comprehensive assessment or as part of a scoring system needs to be more than a proforma version of a thorough history and examination. Oncologists should be persuaded that these data allow for more better definition of the patient within the population but moreover assists shared decision making. There are well validated tools available to oncologists to incorporate features of functional and physical assessment into clinical decision making. The CARG and CRASH tools have been developed to assist higher quality decision making in treating (specifically) older adults. The validation set of the CARG tool was able to predict chemotherapy toxicities for older adults in a way that the KPS was not. The CARG tool has been shown to be practical in application outside of a research setting [68] [69]. The models are built to be used in a clinical environment and can enrich a consent procedure and shared decision making with the patient by incorporating personalised information around fitness and frailty [70] [71] .

The Clinical Frailty Score (developed in Canada by Dr Kenneth Rockwood and team and often named after him) improves on Performance status [72] but like the ECOG scale broadly relies on the core skills of clinical history taking and examination. The CFS provides

greater differentiation than the ECOG PS. It is intended that the CFS be used alongside formal clinical assessment and (ideally) a comprehensive geriatric assessment. It would not be appropriate to define frailty solely on a CFS of 7 or higher without a formal clinical assessment [73]. The CFS is also not validated in patients under the age of 65. Whilst CFS represents an improvement on ECOG PS it should be seen as part of a continuum towards fuller assessment. It is not validated for measuring improvement in individuals after an acute illness for example. In a perfect world the CFS may be seen as a conclusion to a patient focused work up including many of the tools described above, triggered by a PS of >= 2. This needs to be done with the aim of improving the patient's current situation or tackling reversible elements of frailty that may permit oncological treatment – in this context a CGA becomes an oncological Geriatric Assessment. The CFS was never designed ot intended to be an upgrade of ECOG PS but it certainly has benefits. Perhaps the greatest advantage of the CFS is its' widespread use in secondary care. It has been widely adopted throughout acute and emergency medicine in England. The CFS can be used quickly and easily and as a tool, proven to be useable within one minute, was acceptable for use by 75% of emergency department staff in a UK study [74]. Because of the utility of the CFS it has been proposed by NHS England as the preferred triage and assessment tool across the NHS during the Covid-19 pandemic [75]. The CFS has therefore become a tool for recognising frailty using a language that is shared not just within geriatrics or oncology but throughout the hospital ecosystem. This shared language of frailty already gives the CFS an advantage over the ECOG PS – a codified language only spoken and understood within oncology. Recognition of the utility of the CFS in cancer practice has led to the recommendations in the UK that the score recorded as part of standard practice in older women with breast cancer and to large scale pilots of CFS triage in lung cancer chemotherapy clinics [76, 77]

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Conclusions.

Clinical teams should understand that incorporating almost any form of fitness assessment is going to build on the reductive scoring of the ECOG PS. This assessment will require time and workforce to implement correctly. Some of these assessments may take several minutes and a battery of assessments may take up to an hour. A few of these assessments (but not all) would prompt further onward referral for CGA. This should not be positioned as an unreasonable demand as prelude to a treatment that impacts future morbidity and mortality for that patient. We need to move beyond considering these assessments so of function and functional reserve as desirable and to accept them as essential

In an era that promises truly personalised medicine it is no longer appropriate to assess and record patient fitness for treatment with an overly simplified unidimensional tool such as ECOG PS. We cannot make claim to be delivering holistic care with such a limited assessment. Modern oncology is asking way too much of ECOG PS to profile our patients, however the leap to a full Comprehensive (Geriatric) Assessment is asking way too much of our system which lacks the time, resource and expertise required.

Moving to record dimensions of frailty, multimorbidity and functional status should become part of standard clinical and research practice. Usages of these tool will allow for better

consent process. This is likely to be of greatest utility in those patients of PS2 and 3 where the scale provides less granular information.

Oncology teams should familiarise themselves with the domains of frailty and how they are scored and assessed. In collaboration with their colleagues in elderly care and Prehabilitation and rehabilitation professionals formalised assessment should be a part of triaged intervention to optimise fitness and assist the frail.

As clinicians we need to understand what reserve or capacity the patient in front of us has for treatment. Population based statistics can guide us, but we must also understand that there are no 'magic numbers' or scores. What is required is focused use of the tools described above combined with expert and multidisciplinary judgement.

To manage frailty successfully we need a shared language to be communicate across professional groups and within scientific publication. The Clinical Frailty Score has already embedded across secondary care and shown validity in cancer populations and is recommended here for cancer professionals to adopt more widely.

The Clinical Frailty Scale provides a means for oncologists to move beyond the limiting confines of the PS, too long a solely a measure for cancer, and share language with the rest of the hospital in discussing and measuring frailty. Performance Status has served us well but a modern paradigm demands more precision in all aspects of our care – especially evaluation of our patients.

We have an obligation to find the best treatment option for individual patients but also to report and record our outcomes accurately. Spending time making fuller assessment of the patient around the domains of multimorbidity, ageing and frailty is time well spent and is minimal in comparison to the time spent by patients on treatment and by teams in managing toxicity.

Table 1 : Domains and How they may be assessed

Functional Status		ADLS IADLS MOS Physical Functioning ECOG Karnofsky Barthel Index PRISMA-7 MOB-T (for fatigue)
Functional Status (Objective Performance)		TUG Gait speed Short Physical Performance Battery Hand Grip Test Falls history
Psychological health		Geriatric depression score Patient Health Questionnaire PHQ-9 HADS NCCN Distress Thermometer Mental Health Inventory
Multimorbidity		ACE 27 Charlson Comorbidity Index (CCI)

		Klabunde adaptation of the CCI for cancer patients Cumulative Illness Rating Scale
Cognition		MMSE MoCA (more sensitive tool for mild cognitive impairment) [78] Blessed Orientation Memory Concentration Mini-COG Clock drawing test
Polypharmacy		STOP/START
General Screening Tools		Clinical Frailty Score (Rockwood) G8 VES-13 FACT-G Groningen Frailty Score Senior Adult Oncology Program

Figure 1

CASE HISTORY

Well-dressed patient brought to clinic by family

	Patient 1	Patient 2
	75 year old males recently diagnosed with lung cancer. The first patient has been short of breath in the months leading to his diagnosis	
Functional Status	Independent	Needing help with shopping Recent fall
Co-Morbidity	Nil significant	Diabetes Hypertension Ischaemic Heart Disease
Polypharmacy	Takes a statin	5 medications
Nutrition	BMI 29	BM1 19 Recent weight loss of more 3Kg Loss of appetite
Cognition	No issues	Recently more forgetful
Social Status	Attends clinic with wife and daughter	Widower who lives alone
G8 Score	16	5
CFS (Rockwood)	3 (Managing well)	6 (Moderately frail)

myCARG risk of G3-5 toxicity with chemo	59%	86%

Both patients could correctly be assigned a Performance status of 2 but we would expect their tolerance of the same oncological treatment plan to be very different.

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